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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,256	09/13/2005	Angus Moodycliffe	112701-818	3290

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
02/23/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATENTS@BELLBOYD.COM

Office Action Summary	Application No.	Applicant(s)	
	10/525,256	MOODYCLIFFE ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 6-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

In view of the appeal brief filed on December 3, 2008, PROSECUTION IS HEREBY REOPENED. A new ground of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/JD Schultz/

Supervisory Patent Examiner, Art Unit 1635.

Status of Claims

Claims 1-3 and 6-8 are pending and under examination on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, and 6-7 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Walkley et al. (US 2002/0115667 A1).

The claims are drawn to a composition comprising an RNA polynucleotide that is antisense to the glucosylceramide synthase mRNA. The preamble language reciting functional limitations "for preventing or treating epithelial tissue damage" is interpreted as intended use for examination purpose.

Walkley et al. teach an inhibitor of glucosylceramide synthesis, wherein the inhibitor is an RNA antisense molecule that inhibits the expression of glucosylceramide synthase, wherein the inhibitor further comprises a pharmaceutically acceptable carrier. See paragraphs 0013, 0031, 0044, 0051, 0069-0070, 0079. Since the anti-glucosylceramide synthase antisense molecule of Walkley et al. meets the structural requirement set forth in the claims, it necessarily flows that the antisense molecule of Walkley et al. must inherently perform the functions recited in the claims, absent evidence to the contrary. See MPEP 2112, which teaches the following: "[T]he

discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Accordingly, all claim limitations are taught by Walkley et al.

Note that applicant needs to prove that the subject matter shown to be in the prior art does not possess the function of treating or preventing epithelial tissue damage in order to overcome this rejection. See *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980): a case indicating that the burden of proof can be shifted to the applicant to show that the subject matter of the prior art does not possess the characteristic relied on whether the rejection is based on inherency under 35 U.S.C. 102.

Claims 1, 3, and 6-7 are rejected under 35 U.S.C. 102(a) as being anticipated by Di Sano et al. (*Cell Death and Differentiation,* 2002, 9:693-695, citation of record).

The claim is described above.

Di Sano et al. teach a composition comprising an antisense polynucleotide complementary to the glucosylceramide synthase and a physiologically acceptable carrier, wherein the composition downregulates the glucosylceramide synthase activity in cells. Since the anti-glucosylceramide synthase antisense composition of Di Sano et al. meets the structural requirement set forth in the claims, it necessarily flows that the antisense composition of Di Sano

et al. must inherently perform the functions recited in the claims, absent evidence to the contrary. Accordingly, all claim limitations are taught by Di Sano et al.

Claims 1, 3, and 6-7 are rejected under 35 U.S.C. 102(a) as being anticipated by Deng et al. (*Glycobiology,* 2002, 12:145-152, citation of record).

The claim is described above.

Deng et al. teach a composition comprising an antisense polynucleotide complementary to the glucosylceramide synthase and a physiologically acceptable carrier, wherein the composition reduces the glucosylceramide synthase expression in cells. Since the anti-glucosylceramide synthase antisense composition of Deng et al. meets the structural requirement set forth in the claims, it necessarily flows that the antisense composition of Deng et al. must inherently perform the functions recited in the claims, absent evidence to the contrary. Accordingly, all claim limitations are taught by Deng et al.

Claims 1, 3, and 6-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Dwek et al. (US 2002/0142985 A1).

The claims are described above.

Dwek et al. teach an inhibitor of glucosylceramide synthesis, wherein the inhibitor is an RNA antisense molecule that interfers with the expression of glucosylceramide synthase. See paragraphs 0035-0036, 0054, 0061, 0079-0080. Since the anti-glucosylceramide synthase antisense molecule of Dwek et al. meets the structural requirement set forth in the claims, it necessarily flows that the antisense molecule of Dwek et al. must inherently perform the

functions recited in the claims, absent evidence to the contrary. Accordingly, all claim limitations are taught by Dwek et al.

Claims 1, 3, and 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Cabot et al. (WO 01/36628 A1).

The claims are described above.

Cabot et al. teach a composition comprising an antisense nucleic acid that is complementary to the sense strand of the glucosylceramide synthase RNA, wherein the composition inhibits the activity of glucosylceramide synthase. See page 10, 15-19. Since the composition of Cabot et al. meets the structural requirement set forth in the claims, it necessarily flows that the antisense molecule of Cabot et al. must inherently perform the functions recited in the claims, absent evidence to the contrary. Accordingly, all claim limitations are taught by Cabot et al.

Claims 1, 3, and 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al. (*Cell Death and Differentiation,* 2000, 129:667-676, citation of record).

The claim is described above.

Liu et al. teach a composition comprising an antisense polynucleotide complementary to the glucosylceramide synthase and a physiologically acceptable carrier, wherein the composition downregulates the glucosylceramide synthase mRNA and protein expression levels in cells. Since the anti-glucosylceramide synthase antisense composition of Liu et al. meets the structural requirement set forth in the claims, it necessarily flows that the antisense composition of Liu et

al. must inherently perform the functions recited in the claims, absent evidence to the contrary. Accordingly, all claim limitations are taught by Liu et al.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction

provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claims are drawn to a composition for preventing or treating epithelial tissue damage comprising an antisense polynucleotide complementary to the glucosylceramide synthase mRNA.

As such, the claimed composition, provided that patentable weight is given to the preamble intended use language, must impart pharmaceutical or therapeutic effects for any type of epithelial tissue damage. That is, the antisense polynucleotide composition as claimed must prevent (keep from happening or existing, or stop, see the attached dictionary citation) or treat damage of an epithelial tissue of the kidney tubules, lungs, blood vessels, and any organ having an epithelial tissue. However, neither the state of the prior art nor the instant application teaches that the claimed composition that is targeted to and inhibits glucosylceramide synthase indeed treats and prevents any kind of epithelial tissue damage. The only pertinent description with regard to the claimed target gene, glucosylceramide synthase, provided by the disclosure of the specification is that the nucleotide sequence of glucosylceramide synthase was known in the art and that an antisense targeted to glucosylceramide synthase was known to decrease epithelial cell proliferation. See page 10. There is nothing whatsoever that indicates, let alone demonstrates, that inhibition of glucosylceramide synthase can treat and/or prevent any type of epithelial tissue damage. The working examples provided by the specification pertain to the relationship between CD1d expression and skin irritation/inflammation. Such working examples do not represent a clinical association between glucosylceramide synthase and epithelial tissue damage that is required to make and use the claimed therapeutic composition, and there is nothing that shows a

direct link or nexus between the claimed target gene and epithelial tissue damage. Again, there is not even a single prior art reference that teaches or suggests reducing glucosylceramide synthase is useful for treating or preventing epithelial tissue damage, nor has applicant submitted any objective evidence that such knowledge was apparent to one of ordinary skill in the art despite the lack of relevant information in the art at the time the invention was made. Again, as claimed, the claims require that the antisense compound be able to treat and/or prevent any kind of damage (e.g., treating and/or preventing cuts, burns, tears, inflammation) occurred in any type of epithelial tissue (e.g., kidney epithelial tissue, lung epithelial tissue, gland epithelial tissue). However, as stated in the previous Office actions, pharmaceutical utility of antisense compounds for gene therapy was considered unpredictable because of problems and difficulties associated with *in vivo* delivery and *in vivo* pharmacokinetics of the antisense compounds. See the teachings of Opalinska et al. (*Nature Reviews Drug Discovery,* 2002, 1:503-514, citation of record).

In addition, claims 2 and 8 further require that the antisense polynucleotide treatment result in a concurrent reduction in the amount of CD1d in a cell. However, neither the specification nor the state of the prior art establishes the required relationship between reduced glucosylceramide synthase and reduced CD1d. In fact, contrary to the claimed relationship between reduced glucosylceramide synthase and reduced CD1d, it was later found in the art that reduced activity of glucosylceramide, which is synthesized by glucosylceramide synthase, results in the increased expression level of CD1d. See Balreira et al. (*British Journal of Haematology,* 2005, 129:667-676, citation of record). Hence, an antisense polynucleotide against glucosylceramide synthase would increase, not decrease, the amount of CD1d in a cell, which is the opposite effect of the claimed composition.

In view of the foregoing, the quantity of experimentation needed to make and use the invention based on the content of the disclosure would be undue, because the enabling disclosure is not commensurate in scope with the claimed therapeutic composition and because the unpredictability and difficulties associated with *in vivo* activity and delivery of an antisense nucleic acid molecule were fully recognized in the art at the time of the invention. Since the issues described above are not satisfactorily resolved herein, it is concluded, based on the evidence as a whole, that the instant specification fails to teach how to make and use the claimed invention without undue experimentation.

Appellants' arguments filed on December 3, 2008 have been fully considered but are not persuasive. Appellants argue that the working examples showing CD1d knock-out mice fully demonstrate that the specification describes how to make and use the claimed composition. Contrary to appellants' arguments, as stated hereinabove, the working examples pertaining to the relationship between CD1d expression and skin irritation/inflammation are not demonstrative or reflective of therapeutic potential, let alone efficacy, of the claimed antisense composition targeted to glucosylceramide synthase. Further, appellants have failed to show how or why the CD1d-relevant working examples provide sufficient guidance and direction to one of ordinary skill in the art to make and use the claimed invention without undue experimentation. In view of the reasons stated above, this rejection is reapplied herein.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner, Art Unit 1635